REMARKS

Status Summary

Claims 150-164, 167-174, 177-210, 213-222, 227-233, 236-251, and 257-268 are identified as pending and under examination. Claims 150-153, 158-164, 167-174, 181-199, 204-210, 213-222, 227-233, 236-243, and 248-251 are identified as allowed. Although not indicated as such in the official action, claims 188-189 were canceled previously, and therefore, it is understood that these claims are neither pending nor allowed. Claims 154-157, 177-180, 200-203, and 244-247 are subject to an objection under 37 CFR 1.75(c) as allegedly being of improper dependent form. Claims 177-180, 200-203, 244-247, and 257-268 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Claims 154-157, 177-180, 200-203, 244-247, and 257-268 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to meet the written description requirement by introducing new matter.

Claims 153-157, 177-180, 222, and 257-268 are canceled herein without prejudice. Claims 151, 174, 197, 199-203, 220, and 243-247 are amended. No new matter is added by the amendments. Reconsideration is respectfully requested in view of the claim amendments, claim cancellations, and following remarks.

Summary of Interview with Examiner

A telephonic interview with Examiner Brandon Fetterolf and applicants' representatives, Julie Broadus Meigs and Linda Sigillito Hutchison, took place on 11 January 2010. Applicants wish to thank Examiner Fetterolf for his time and consideration in discussing the outstanding rejections.

Amendment to the Drawings

A substitute Figure 6 was submitted with the response filed 7 August 2009. Applicants note that the official action does not acknowledge that the substitute Figure 6 was deemed acceptable. Applicants respectfully request that the examiner confirm consideration of the substitute Figure 6.

Claim Objections

Claims 154-157, 177-180, 200-203, and 244-247 are subject to an objection under 37 CFR 1.75(c) as allegedly being of improper dependent form for failing to further limit the subject matter of a previous claim. Official action, page 2.

Initially, applicants respond that claims 154-157 and 177-180 are canceled without prejudice, and therefore, the objection is moot with respect to these claims. Applicants further respond that independent claims 196 and 242 describe an anti-CD22 antibody by reference to CDR sequences, and that dependent claims 200-203 and 244-247 limit the scope of claims 196 and 242 by specifying particular sequences of the framework regions. Therefore, it is believed that claims 200-203 and 244-247 properly depend from base claims 196 and 242, respectively, and it is respectfully requested that the objection be withdrawn.

Rejection of Claims Under 35 U.S.C. § 112, Second Paragraph

Claims 177-180, 200-203, 244-247, and 257-268 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctively claim the subject matter which applicant regards as the invention. With respect to claims 177-180, the examiner sates that the description "heavy chain variable region" lacks antecedent basis. With respect to claims 200-203 and 244-247, the examiner states that the claims do not describe the structure of the antibody and comprise an infinite number of possible sequences. With respect to claims 257-268, the examiner states that the claims do not further limit the antibody described in claim 196. Official action, pages 2-3.

Initially, as noted herein above, claims 177-180 and 257-268 are canceled without prejudice, and therefore, the rejection is moot with respect to these claims. The cancellation of claims does not indicate acquiescence with the stated reasons for rejection, but rather, is only for the purpose of facilitating issuance of the allowed claims.

Claims 200-203 and 244-247 are amended to clarify particular framework sequences of the antibodies. The amendments clarify the relationship of the positions of the backmutations within the framework regions and specify a finite number of complete variable region sequences, as described further below.

Specifically, claims 200, 201, 244, and 245 are amended to clarify that the positions of the backmutations described therein are at linearly numbered residues of SEQ ID NO:8, which is

the donor sequence for CDRs of the heavy chain variable region identified in base claim 196, and that all other residues of the framework region are occupied by *corresponding* residues of the acceptor framework sequences set forth as SEQ ID NOs:21 and 22. Figure 6 provides a sequence alignment of antibody heavy chain variable regions described in the application, including SEQ ID NO:8 (V_H of the 5/44 donor antibody), SEQ ID NO:21 (human DP7 acceptor framework), and SEQ ID NO:22 (human JH4 acceptor framework). As shown in Figure 6 and by reference to the sequence listing, linear residues 1-30 of SEQ ID NO:8 correspond to linear residues 1-30 of SEQ ID NO:21; linear residues 36-49 of SEQ ID NO:8 correspond to linear residues 31-44 of SEQ ID NO:21; linear residues 67-98 of SEQ ID NO:8 correspond to linear residues of 49-80 of SEQ ID NO:21; and linear residues 111-121 of SEQ ID NO:8 correspond to linear residues 1-11 of SEQ ID NO:22. Accordingly, the positions in SEQ ID NOs:21 and 22, which correspond to the positions of backmutations identified in the claims with reference to SEQ ID NO:8, and all remaining residues of the framework, are believed to be clear.

Claims 202, 203, 246, and 247 are amended to clarify that the positions of the backmutations described therein are at linearly numbered residues of SEQ ID NO:7, which is the donor sequence for CDRs of the light chain variable region identified in base claim 196, and that all other residues of the framework region are occupied by *corresponding* residues of the acceptor framework sequences set forth as SEQ ID NOs:17 and 18. Figure 5 provides a sequence alignment of antibody light chain variable regions described in the application, including SEQ ID NO:7 (V_L of the 5/44 donor antibody), SEQ ID NO:17 (human DPK9 acceptor framework), and SEQ ID NO:18 (human JK1 acceptor framework). As shown in Figure 5, linear residues 1-23 of SEQ ID NO:7 correspond to linear residues 1-23 of SEQ ID NO:17; linear residues 40-54 of SEQ ID NO:7 correspond to linear residues 24-38 of SEQ ID NO:17; linear residues 62-93 of SEQ ID NO:7 correspond to linear residues 39-70; and linear residues 103-113 of SEQ ID NO:7 correspond to linear residues 1-11 of SEQ ID NO:18. Accordingly, the positions in SEQ ID NOs:17 and 18, which correspond to the positions of backmutations identified in the claims with reference to SEQ ID NO:7, and all remaining residues of the framework, are believed to be clear.

Based upon the foregoing, it is believed that the amended language of claims 200-203, 244-247 has a clear meaning readily understood by one skilled in the art, and it is respectfully requested that the rejection of claims under 35 U.S.C. § 112, second paragraph, be withdrawn.

Rejection of Claims Under 35 U.S.C. § 112, First Paragraph – New Matter

Claims 154-157, 177-180, 200-203, 244-247, and 257-268 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to meet the written description requirement by introducing new matter. With respect to claims 154-157 and 177-180, the examiner states that the specified backmutations are not described in the originally filed application. With respect to claims 200-203 and 244-247, the examiner states that the description of residues of SEQ ID NOs:7 and 8 without reference to a particular framework region is not described in the originally filed application. With respect to claims 257-268, the examiner suggests that the claims encompass CDR-H2 species not described in the originally filed application. Official action, pages 4-5.

Applicants initially respond that, as noted herein above, claims 153-157, 177-180, and 257-286 are canceled without prejudice, and therefore, the rejection is moot with respect to these claims. The cancellation of claims does not indicate acquiescence with the stated reasons for rejection, but rather, is only for the purpose of facilitating issuance of the allowed claims.

Applicants further respond that claims 200-203 and 244-247 are amended to clarify the particular heavy chain and light chain variable region variants encompassed by the claims and depicted in Figures 5 and 6. The comments above in response to the rejection of claims under 35 U.S.C. § 112, second paragraph, are incorporated herein as also responsive to the rejection of the same claims under 35 U.S.C. § 112, first paragraph.

In addition, the strategy for preparation of humanized anti-CD22 antibodies is described in Example 2 of the originally filed specification (pages 50-51). As referenced in Example 2, the amino acid sequence of the murine 5/44 donor light chain variable region, V_L, is depicted in Figure 5 and is also set forth as SEQ ID NO:7. The acceptor framework regions for constructing the CDR-grafted light chain correspond to those of the human VK sub-group I germline O12, DPK9 sequence, which is also set forth as SEQ ID NO:17. The framework 4 acceptor sequence was derived from the human J-region germline sequence JK1, which is set forth as SEQ ID NO:18. Applicants describe a comparison of the amino acid sequences of the light chain framework regions of the murine 5/44 donor antibody and the human acceptor framework regions. This comparison resulted in identifying 27 differences between the donor and acceptor sequences. Following grafting of murine CDRs onto the human frameworks, murine framework residues considered potentially important to antigen binding and/or sufficiently different from

the corresponding human residue in terms of size, polarity or charge, were reintroduced as backmutations. Representative light chain variable region sequences containing such backmutations are depicted as humanized variants gL1 and gL2 in Figure 5.

Also described in Example 2, the amino acid sequence of the murine 5/44 donor heavy chain variable region, V_H, is depicted in Figure 6 and is also set forth as SEQ ID NO:8. The acceptor framework regions for constructing the CDR-grafted heavy chain correspond to those of the human VK sub-group I germline VH1-3, DP7 sequence, which is set forth as SEQ ID NO:21. The framework 4 acceptor sequence was derived from the human J-region germline sequence J4, which is set forth as SEQ ID NO:22. Applicants describe a comparison of the amino acid sequences of the heavy chain framework regions of the murine 5/44 donor antibody and the human acceptor framework regions. This comparison resulted in identifying 22 differences between the donor and acceptor sequences. Following grafting of murine CDRs onto the human frameworks, murine framework residues considered potentially important to antigen binding and/or sufficiently different from the corresponding human residue in terms of size, polarity or charge, were reintroduced as back mutations. Representative heavy chain variable region sequences containing such backmutations are depicted as humanized variants gH1, gH4, gH5, gH6, and gH7 in Figure 6.

Based upon the foregoing, it is believed that claims 200-203 and 244-247 are fully supported by the originally filed application, and it respectfully requested that the rejection of claims under 35 U.S.C. § 112, first paragraph, be withdrawn.

Additional Claim Amendments

In addition to the amendments described herein above, the claims are further amended as follows:

Claims 151, 174, 197, and 220 are amended to delete the language "or a heavy chain monomer or dimer" as inconsistent with the elements set forth in the base claim. Claim 174 is additionally amended to further delete the term "Fv," and claim 220 is amended to delete the phrases "a human antibody" and "a humanized antibody," for the same reasons.

Claim 153 is canceled.

Claims 199 and 243 are amended to delete the language "and non-human donor CDRs." The amendment is made to clarify that the base claims 196 and 242 set forth particular CDR

sequences, all of which are non-human donor CDRs, and dependent claims 199 and 243 do not improperly expand this subject matter.

Claim 222 is canceled.

Conclusion

All rejections having been addressed, it is respectfully submitted that the present application is in condition for allowance and a notice to that effect is earnestly solicited. If any points remain in issue, which may be best resolved through a personal or telephone interview, the examiner is kindly requested to contact the undersigned attorney at the telephone number listed below.

Respectfully submitted,

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